

### Remarks

The August 25, 2004 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set in the August 25, 2004 Official Action. Therefore, the initial due date for response was November 25, 2004. A petition for a two month extension of the response period is presented with this response, which is being filed within the two month extension period.

As another preliminary matter, it is noted that the Examiner has maintained and made final the requirement for restriction in the April 6, 2004 Official Action. Applicants wish to make clear that the election of claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 in response to the aforementioned requirement for restriction is without prejudice to their rights to file one or more divisional applications, as provided in 35 U.S.C. §121, directed to the subject matter of the claims held finally withdrawn from consideration in this application.

At pages 4-6 of the instant Official Action, the Examiner has objected to the specification on several grounds. Specifically, the Examiner has objected to the specification for not providing sequence identifiers throughout the specification, allegedly failing to provide a descriptive title, failing to properly title the section Brief Description of the Drawings, and allegedly providing an incomplete citation at page 40, line 1. In response to the Examiner's objections, Applicants have inserted sequence identifiers throughout the specification, replaced the original title with the title suggested by the Examiner, inserted the heading "Brief Description of the Drawings," and deleted the incomplete citation at page 40, line 1. Applicants note that

the deleted citation was originally included merely to provide background information on the well known vector pUC18. Inasmuch as pUC18 was a well known vector at the time the instant invention was made, Applicants submit that the deletion of this reference does not raise any issues of enablement, adequate written description, or new matter. Applicants have also adopted the Examiner's suggestion and replaced the sequences provided in Table II at pages 70-99 with sequence identifiers. Applicants also note that the sequences present throughout the specification were properly included in the sequence listing as previously filed. Accordingly, Applicants submit that a new sequence listing is not required.

Additionally, the Examiner has objected to the amendment filed November 28, 2001 under 35 U.S.C. §132 for allegedly adding new matter to the specification. It is the Examiner's position that the term "a polyketide other than monensin," which was added to claims 22 and 26, lacks support. Applicants respectfully disagree with the Examiner. As originally presented, claim 22 recited the "use of a portion of the monensin gene cluster ... in the synthesis of a polyketide other than monensin." Original claim 26 comprises similar language. Accordingly, Applicants submit that the amendments to claims 22 and 26 are fully supported by the claims as originally presented. Applicants respectfully request the new matter objection be withdrawn.

Claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 have been objected to for allegedly containing non-elected subject matter. Claim 1 has also been objected to for improper punctuation. Applicants submit that the currently pending claims have been amended to remove non-elected subject matter and recite all, or a portion of the monAIV gene. Applicants have also amended claim 1 to provide proper punctuation, in accordance with the Examiner's suggestion.

The Examiner has also rejected claims 6, 7, 11, 30-34, 37, and 38 under 35 U.S.C. §112, second paragraph for alleged indefiniteness.

Additionally, claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 have been rejected for allegedly failing to satisfy the written description requirement of 35 U.S.C. §112, first paragraph. The Examiner has also rejected claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

At page 15 of the Official Action, the Examiner has rejected claims 1-3, 6-9, 46, and 47 under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter.

Claims 1, 3, 6-10, 12, and 47 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by GenBank Accession No. AF144047 and as allegedly being anticipated by GenBank Accession No. U78289.

Lastly, the Examiner has rejected claims 11, 30-34, 37, and 38 under 35 U.S.C. §102(b) as allegedly being anticipated by Kuhstoss et al. (Gene (1996) 183:231-236).

The foregoing objections and rejections constitute all of the grounds set forth in the August 25, 2004 Official Action for refusing the present application.

Claim 6 has been cancelled and claims 48 and 49 have been added in accordance with this amendment. Support for new claim 48 can be found at Table I at page 68, line 43. Support for new claim 49 can be found at page 56, lines 3-8 and original claim 28.

Applicants have also amended claims 1-3, 7, 8, 11, 30, 32, 34, and 46. Claims 2, 7, 8, 11, 30, 32 and 46 have been amended so that the claim are more clearly directed to the elected species of sequences comprising at least part of monAIV gene. Applicants submit that support for the amendments to these claims is inherent in the claims as previously filed. Support for the amendment to claim 1 can be found throughout the specification, including at original

claims 6-8 and at Table I from page 68, line 43 through page 69, line 6. Support for the amendment to claim 3 can be found at page 18, line 16 through page 19, line 4. Support for the amendment to claim 34 can be found at original claim 27 and in Example 7 (pages 55-58).

No new matter has been introduced into this application by reason of any of the amendments presented herewith.

For the reasons set forth below, Applicants respectfully submit that the various objections to the specification and claims, the 35 U.S.C. §112, first paragraph rejections of claims 1-3, 6-12, 30-34, 37, 38, 46, and 47, the 35 U.S.C. §112, second paragraph rejections of claims 6, 7, 11, 30-34, 37, and 38, the 35 U.S.C. §101 rejection of claims 1-3, 6-9, 46, and 47, and the 35 U.S.C. §102(b) rejections of claims 1-3, 6-12, 30-34, 37, 38, and 47, as set forth in the August 25, 2004 Official Action, either lack merit or cannot be maintained in view of the present amendment. These grounds of objection and rejection are, therefore respectfully traversed.

**CLAIMS 6, 7, 11, 30-34, 37, AND 38, AS AMENDED, SATISFY THE REQUIREMENTS OF 35 U.S.C. §112, SECOND PARAGRAPH**

The Examiner has rejected claims 6, 7, 11, 30-34, 37, and 38 under 35 U.S.C. §112, second paragraph for alleged indefiniteness. Specifically, it is the Examiner's position that (1) the term "polypeptides set out below" in claim 6 lacks antecedent basis, (2) the term "polyketide synthase multienzyme" in claim 6 is a name and not an activity as the claim indicates, (3) the term "corresponding polyketide" in claim 11 is unclear, (4) the abbreviations "PKS" and "AT" recited in claim 30 are not previously spelled out, (5) the terms "said modules or a domain" and "an ery loading module" in claim 30 are unclear, and (6) the term "derived from" in claim 34 is unclear.

Applicants have cancelled claim 6 thereby rendering moot the rejections of this claim. Applicants note that claim 7, which previously depended from claim 6, does not contain any of the allegedly indefinite terms as currently amended.

With regard to claim 11, Applicants have amended the claim to recite that the transformant cell is capable of "expressing the polypeptide encoded for by said DNA sequence" instead of "expressing a corresponding polypeptide." Applicants submit that this amendment to claim 11 eliminates any ambiguity that may have existed regarding the recited polypeptide.

Applicants have amended claim 30, from which claims 31-33, 37, and 38 depend, to provide the full length names of PKS and AT prior to using the abbreviations in the remainder of the claim. Applicants have also adopted the Examiner's helpful suggestion and amended claim 30 to replace "an ery loading module" with "the erythromycin loading module." Applicants have also replaced the abbreviation "ery" with the full length name "erythromycin" throughout the claim. Additionally, to clarify which modules and domains are contiguous in claim 30, Applicants have amended the claim to clearly recite that the at least one module or domain from MonAIV is contiguous to the PKS loading module or the further PKS extension module or domain, which is not naturally contiguous to the at least one module or domain from MonAIV. Notably, dependent claims 31-33, 37, and 38 do not recite any of the allegedly indefinite terms.

Lastly, Applicants have amended claim 34 to recite that the loading module is a "KSq domain derived from a ketosynthase (KS) domain of a monensin extension module." Applicants submit that claim 34, as currently amended, clearly identifies the starting material as a KS domain of a monensin extension module, the end material as a KSq domain, and the changes allowed by the term "derived from" as any means to achieve the KSq domain. Accordingly, Applicants respectfully

submit that the metes and bounds of claim 34, as amended, cannot be reasonably held to be indefinite.

In light of all the foregoing, Applicants submit that each of the rejections of claims 6, 7, 11, 30-34, 37, and 38 under 35 U.S.C. §112, second paragraph for alleged indefiniteness has been overcome. Accordingly, Applicants respectfully request that the rejections be withdrawn.

**CLAIMS 1-3, 6-12, 30-34, 37, 38, 46, AND 47, AS AMENDED,  
SATISFY THE WRITTEN DESCRIPTION REQUIREMENT OF 35 U.S.C. §112,**

**FIRST PARAGRAPH**

The Examiner has rejected claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 for allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph. The Examiner contends that the specification has not fully described a genus of polynucleotides satisfying the identity limitations set forth in claim 1 in the absence of functional limitations. Furthermore, the Examiner asserts that there is inadequate support for the term "allele, mutation, or other variant," recited in claim 3, in the absence of any structural limitations. It is also the Examiner's position that claim 30 is drawn to nucleic acid molecules based solely on function without any structure limitations.

Applicants respectfully disagree with the Examiner and submit that the instant application provides more than adequate written description for alleles, mutants, and other variants of the claimed DNA sequences. However, in the interest of expediting prosecution, Applicants have amended claim 1 to remove reference to variant sequences comprising at least 80% identity with the peptides set forth in Table II. As currently amended, claim 1 is drawn to DNA sequences which encode for at least part of MonAIV, wherein the at least part of MonAIV is a polypeptide having at least one enzymatic activity. Inasmuch as Table I defines the nucleotide regions

of the enzymatic domains and Table II provides the amino acid sequences of the monensin gene cluster, Applicants respectfully submit that the specification provides an adequate written description of the full scope of the claimed chemical compounds.

Applicants have also amended claim 3 to recite a DNA sequence encoding for MonAIV. Inasmuch as claim 3, as amended, clearly provides the structure of the recited DNA sequence, Applicants submit that the instant rejection has been overcome.

With regard to independent claim 30, Applicants have amended the claim to recite that the DNA sequence comprises "a monensin module or domain from monAIV." Applicants submit that claim 30, as amended, clearly recites a structural feature of the claimed invention and no longer can be reasonably held to describe the claimed DNA by only functional language.

In light of the foregoing, Applicants submit that each of the rejections of independent claims 1 and 30 and dependent claims 2, 3, 6-12, 31-34, 37, 38, 46, and 47 for allegedly failing the written description of 35 U.S.C. §112, first paragraph for alleged indefiniteness have been overcome. Accordingly, Applicants respectfully request that the rejections be withdrawn.

**CLAIMS 1-3, 6-12, 30-34, 37, 38, 46, AND 47, AS AMENDED,  
SATISFY THE ENABLEMENT REQUIREMENT OF 35 U.S.C. §112, FIRST  
PARAGRAPH**

The Examiner has rejected claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 for allegedly failing to satisfy the enablement requirement under 35 U.S.C. §112, first paragraph. Specifically, the Examiner contends that the specification fails to provide enablement for DNA fragments with as little as 80% sequence identity to monAIV.

In the interest of expedited prosecution, Applicants have amended the currently pending claims to recite DNA sequences which encode for at least part of MonAIV. Indeed, independent claim 1 is drawn to DNA sequences encoding for at least part of MonAIV wherein the at least part is a polypeptide having an enzymatic activity. Language pertaining to DNA sequences having 80% sequence identity to monAIV has been removed from claim 1. Additionally, the term "or variant thereof" has been removed from independent claim 30.

Inasmuch as the DNA sequences recited in independent claims 1 and 30 encode for at least part of MonAIV and claims 2, 3, 6-12, 31-34, 37, 38, 46, and 47 depend from either claim 1 or 30, Applicants submit that claims 1-3, 6-12, 30-34, 37, 38, 46, and 47, as amended, are fully enabled. Accordingly, Applicants respectfully request the instant rejection be withdrawn.

**CLAIMS 1-3, 6-9, 46, AND 47, AS AMENDED, ARE DIRECTED TO  
STATUTORY SUBJECT MATTER**

The Examiner has rejected claims 1-3, 6-9, 46, and 47 under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter. It is the Examiner's position that the claims as written do not sufficiently distinguish over nucleic acid molecules as they naturally exist.

Applicants have adopted the Examiner's suggestion and amended independent claim 1 to recite that the DNA sequences are isolated. Inasmuch as claims 2, 3, 6-9, 46 and 47 depend from claim 1, Applicants submit the instant rejection has been overcome. Applicants respectfully request the withdrawal of the rejection of these claims under 35 U.S.C. §101.



**CLAIMS 1, 3, 6-10, 12, AND 47, AS AMENDED, ARE NOT ANTICIPATED BY GENBANK ACCESSION NUMBERS AF144047 OR U798289 AND CLAIMS 11, 30-34, 37, AND 38 ARE NOT ANTICIPATED BY KUSTOSS ET AL.**

Claims 1, 3, 6-10, 12, and 47 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by GenBank Accession No. AF144047 (hereinafter AF144047) and as allegedly anticipated by GenBank Accession No. U78289 (hereinafter U78289). The Examiner has also rejected claims 11, 30-34, 37, and 38 under 35 U.S.C. §102(b) as allegedly anticipated by Kuhstoss et al. (Gene (1996) 183:231-236).

AF144047 teaches a 740 basepair *S. cinnamomensis* sequence having a stretch of 21 nucleotides which are identical to the nucleotide sequence of *monAIV* presented in SEQ ID NO: 2 of the instant application. By contrast, claim 1, as now amended, recites DNA sequences encoding for at least part of MonAIV, wherein the part of MonAIV is a polypeptide having at least one enzyme activity selected from the group consisting of ketosynthase activity, acyl transferase activity, dehydratase activity, ketoreductase activity, acyl-carrier protein activity, and enoyl reductase activity. A review of AF144047 and the sequence alignments provided by the Examiner clearly reveals that the amino acid sequence encoded for by AF144047 does not comprise a polypeptide of MonAIV having at least one enzyme activity. Indeed, the sequence alignments provided by the Examiner show that the greatest homology between AF144047 and SEQ ID NO: 2 of the instant application is from nucleotides 42714-42960 and from nucleotides 48058-48328 of SEQ ID NO: 2. Notably, nucleotides 42714-42960 lie within but do not encompass the ketosynthase 5 domain which spans from nucleotides 42628-43890 of MonAIV, and nucleotides 48058-48328 lie within but do not encompass the ketosynthase 6 domain which spans from nucleotides 47947-49218 of MonAIV, as indicated by Table I of the instant application.

Thus, while the nucleotide sequence described by AF144047 has limited regions of homology with SEQ ID NO: 2 of the instant application, AF144047 fails to describe a DNA sequence which encodes a monAIV polypeptide having one of certain enzymatic activities, as required by amended claim 1. Inasmuch as AF144047 fails to teach each and every aspect of the instantly claimed invention, Applicants submit that the rejection of claims 1, 3, 6-10, 12, and 47 under 35 U.S.C. §102(b) as allegedly being anticipated AF144047 has been overcome.

U78289 allegedly teaches a 43280 basepair *S. fradiae* ty lactone synthase sequence having a stretch of 39 nucleotides which are identical to the nucleotide sequence of *monAIV* presented in SEQ ID NO: 2 of the instant application. A review of U78289 and the sequence alignments provided by the Examiner clearly reveals, however, that the amino acid sequence encoded for by U78289 does not comprise a polypeptide of MonAIV having at least one enzyme activity. Indeed, while the nucleotide sequence taught by U78289 has limited regions of homology with the monAIV portion of SEQ ID NO: 2 of the instant application and encodes for short amino acid sequences which are a part of MonAIV, none of the amino acid sequences of complete homology are long enough to comprise a polypeptide having a certain enzymatic activity, as required by the instant claims. Accordingly, Applicants respectfully submit that U78289 cannot be reasonably held to anticipate claims 1, 3, 6-10, 12, and 47.

The Examiner alleges that claims 11, 30-34, 37, and 38 are anticipated by Kuhstoss et al. It is the Examiner's position that Kuhstoss et al. teach a polyketide synthase comprising the loading module of the ty lactone polyketide synthase, a monensin variant, and extension modules of the platenolide I polyketide synthase. Applicants submit, however, that the ty lactone polyketide synthase module is not a "monensin variant" module. As set forth above, Applicants have deleted reference to MonAIV variants from claim 30.

Accordingly, the instantly claimed invention requires that the polyketide synthase comprise a module or domain from MonAIV. Inasmuch as Kuhstoss et al. clearly fail to describe a polyketide synthase having a module or domain from MonAIV, Applicants submit that Kuhstoss et al. cannot be reasonably held to anticipate the instantly claimed invention.

In light of all the foregoing, Applicants respectfully request the withdrawal of the rejections of claims 1, 3, 6-10, 12, and 47 under 35 U.S.C. §102(b) as allegedly anticipated by AF144047 and U78289, and of claims 11, 30-34, 37, and 38 under 35 U.S.C. §102(b) as allegedly anticipated by Kuhstoss et al.

#### CONCLUSION

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the August 25, 2004 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,  
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